5A
7/8/02

UNITED STATES PATENT AND TRADEMARK OFFICE

In re Appln of:	Dr. Eduard Lerner		
Ser No:	10/050,183	Group Art Unit:	
Filed:	January 18, 2002	Examiner:	
For:	Methods and Apparatus For Enhanced and Controlled Delivery of Biologically Active Agent Into the Central Nervous System Of A Mammal		
Atty. Dkt:	10087-P04cip2		

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

PRELIMINARY AMENDMENT

Kindly amend the application by adding the following claims:

13.. A method, using an implantable device, for enhanced and controlled delivery of a biologically active agent into the spinal structures and/or the brain of a mammal, particularly a human being, and that circumvents the systemic circulation, which comprises the steps of:

cv

(i) directing at least one end of a catheter containing a delivery device to the epidural space of a mammal and positioning said catheter and delivery device within the epidural space to provide an effective arrangement for delivering a biologically active agent which is contained in said device into the mammal;

(ii) advancing a first electrode from said delivery device that is constructed and arranged to be positioned in the epidural space of a mammal into the epidural space of a mammal and act as a donor electrode;

(iii) applying a second electrode that is constructed and arranged to be positioned at a determined internal or external position of the mammal's body and act as a receptor electrode;

(iv) electrically connecting said first and second electrodes to a power control unit that includes an integrated (pre)-programmable power source, the power source being operated by a microprocessor, said power source providing a potential gradient so that delivery of a biologically active agent is accomplished in a direction from said first electrode directly

into the spinal structures and/or the brain thereby essentially bypassing the systemic circulation of a mammal; and

(v) delivering said biologically active agent to the spinal structures and/or to the brain of said mammal using an active transport means.

14. A method according to claim 13 wherein the active transport means is iontophoresis and/or phonophoresis.

15. A method according to claim 13 wherein said power source provides an electro-potential gradient or ultrasound.

16. A method as claimed in claim 13 wherein a biosensor is connected to the power control unit for feedback regulated delivery of a biologically active agent to the spinal structures and/or the brain of a mammal.

17. A method as claimed in claim 16 wherein the biosensor is adapted to register biopotentials for feedback regulated delivery of a biologically active agent in the treatment of chronic pain, hyperkinesis or any other pathological symptoms or diseases.

18. A method as claimed in claim 13 wherein the donor electrode includes a drug reservoir or drug transfer part for storage of the biologically active agent, an impermeable part that is not involved in drug transfer, and an electroconductive member.

19. A method as claimed in claims13 wherein the receptor electrode is an iontophoresis electrode which includes an electrolyte-containing compartment for storage of electrolyte, an electroconductive member and a membrane through which electrolyte transport occurs.

20. A method according to claim 13 that includes a means for in situ refilling of said device.

21. A method as claimed in claim 13 wherein the donor electrode includes a means for expansion thereby allowing the drug reservoir or transfer part to make an intimate contact with the dura mater.

22. A method as claimed in claim 13 wherein an expansion means is operably connected to the drug delivery device, the expansion means being configured to expand the donor electrode in a direction substantially radial thereby promoting an improved contact interface between the drug reservoir or transfer part and the dura mater.

23. A method as claimed in claim 20 wherein an expansion means is provided by reversible swelling properties of the drug reservoir or transfer part that is induced by chemical or physical changes such as for example, electric current, pH, temperature or any combinations thereof.

24. A method as claimed in claim 13 wherein the drug delivery part of the device is shaped following expansion according to the human epidural space.

25. A method according to claim 13 wherein said first electrode is a reservoir-type iontophoresis electrode holding a supply of the selected biologically active agent in a formulation suitable for iontophoretic or phonophoreticdelivery and/or wherein said second electrode is a reservoir-type iontophoresis electrode holding a supply of electrolyte.

26. A method according to claim 13, wherein said first and second electrodes comprises an electroconductive part having electroconductive material selected from the following group: stainless steel, gold, silver, titanium, copper, zinc, graphite and metal salts (e.g. silver chloride).

27. A method according to claim 13 wherein said reservoir of said first and/or second electrode means is formed of a polymer matrix containing an electroconductive filler material selected from the group consisting of a metal powder, powdered graphite and carbon fibers.

28. A method according to claim 25 wherein said reservoir is constructed of material that is adapted to absorb, hold and release the biologically active agent and/or electrolyte.

29. A method according to claim 25 wherein said reservoir is made of a hydrogel that holds the biologically active agent and/or electrolyte.

30. A method according to claim 13 wherein the catheter-based device includes a mean for endoscopic controlled installation such as an optic fiber.

31. A method according to claims13 wherein the catheter-based device can be removed entirely from the epidural space following positioning of the donor electrode.